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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Our Case No. 00-1086-G)

In re Application of: )  
)  
Letsinger, et al. )  
)  
Serial No. 10/633,878 ) Examiner: TBA  
)  
Filed: August 4, 2003 ) Group Art Unit: 1645  
)  
For: Method of Detection By Enhancement ) Confirmation No.: 5233  
of Silver Staining )

**TRANSMITTAL LETTER**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 2231-1450

Sir:

In regard to the above identified application.

1. We are transmitting herewith the attached:

- a) Sixth Supplemental Information Disclosure Statement
- b) U.S. PTO 1449 Form with copies of 29 references; and
- c) Return Postcard.

2. With respect to additional fees:

A check in the amount of \$0.00 is attached.

3. **GENERAL AUTHORIZATION:** Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.

4. **CERTIFICATE OF MAILING UNDER 37 CFR § 1.8:** The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 9 day of July, 2004.

Date:

July 9, 2004

Respectfully submitted,

Emily Miao  
Registration No. 35,285



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**(Our Case No. 00-1086-G)**

## PATENT

re Application of:

Letsinger, et al.

Serial No. 10/633,878

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For: Method of Detection By Enhancement  
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Examiner: TBA

Art Unit: 1645

Confirmation: 5233

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

## SIXTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies<sup>1</sup> of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. Merrill, et al., U.S. Patent No. 5,830,986, issued November 3, 1998.
2. Lough, et al., U.S. Patent No. 5,900,481, issued May 4, 1999.

<sup>1</sup>To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated therebetween; if no such English language equivalent is cited, then none is known to undersigned.

3. Goldberg, et al., U.S. Patent No. 6,203,989, issued March 20, 2001
4. Bawendi, et al., U.S. Patent No. 6,251,303, issued June 26, 2001.
5. Abbott, et al., U.S. Patent No. 6,277,489, issued August 21, 2001.
6. Bawendi, et al., U.S. Patent No. 6,306,610, issued October 23, 2001
7. Mirkin, et al, U.S. Patent No. 6,361,944, issued March 26, 2002.
8. Wagner, et al., U.S. Patent No. 6,365,418, issued April 02, 2002
9. Mirkin, et al., U.S. Patent No. 6,417,340, issued July 09, 2002
10. WO 93/25709 published 23 December 1993.
11. WO 98/04740 published 5 January 1998
12. WO 98/17317 published 30 April 1998
13. WO 99/60169 published 25 November 1999
14. WO 00/33079 published 8 June 2000
15. WO 01/00876 published 4 January 2001
16. WO 01/51665 published 19 July 2001
17. WO 01/73123 published 4 October 2001
18. WO 01/86301 published 15 November 2001
19. WO 02/04681 published 17 January 2002
20. WO 02/18643 published 7 March 2002
21. WO 02/36169 published 10 May 2002
22. WO 02/46483 published 13 June 2002
23. WO 02/46472 published 13 June 2002
24. Letsinger, R., et al., "Chemistry of Oligonucleotide-Gold Nanoparticle Conjugates," *Phosphorus, Sulfur and Silicon*, Volume 144, p. 359-362 (1999)

25. Letsinger, R., et al., "Use of a Steroid Cyclic Disulfide Anchor in Constructing Gold Nanoparticle—Oligonucleotide Conjugates," *Bioconjugate Chem*, p. 289-291 (2000)
26. Li Z., et al., "Multiple thiol-anchor capped DNA-gold nanoparticle conjugates," *Nucleic Acids Research*, Volume 30, p. 1558-1562 (2002)
27. Nuzzo R., et al., "Spontaneously Organized Molecular Assemblies. 3. Preparation and Properties of Solution Adsorbed Monolayers of Organic Disulfides on Gold Surfaces," *J. Am Chem. Soc.*, Volume 109, p. 2358-2368 (1987)
28. Otsuka, H, et al., "Quantitative and Reversible Lectin-Induced Association of Gold Nonoparticles Modified with  $\alpha$ -Lactosyl- $\omega$ -mercapto-poly(ethyleneglycol)," *J. Am Chem. Soc.*, Volume 123, p. 8226-8230 (2001).
29. Wuelfing, P, et al, "Nanometer Gold Clusters Protected by Surface-Bound Monolayers of Thiolated Poly(ethylene glycol) Polymer Electrolyte," *J. Am. Chem. Soc.*, Volume 120, p. 12696-12697 (1998)

In accordance with MPEP Sections 609 and 707.05(b), it is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended

that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Dated: July 9, 2004

Respectfully submitted,

  
\_\_\_\_\_  
Emily Miao  
Registration No. 35,285

McDonnell Boehnen Hulbert & Berghoff LLP  
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Chicago, Illinois 60606  
Telephone : (312) 913-0001  
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**PATENT**

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**(Our Case No. 00-1086-G)**

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**FIFTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

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1. International Application No. WO 92/04469, published 19 March 1992
2. International Application No. WO 90/02205, published 8 March 1990
3. Borman, *Chem.Eng. News*, December 9, 1996, pp. 42-43 (1996)

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4. Tomlinson et al. *Anal Biochem*, Vol. 171, pp. 217-222 (1988)

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Early and favorable consideration is earnestly solicited.

Dated: May 9, 1991

Respectfully submitted,

  
Emily Miao

Registration No. 35,285

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FORM PTO-1449  
(Rev. 2-32)

U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.

00-1086-G

Serial No.

10/633,878

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Letsinger, et al.

Filing Date:

August 4, 2003

Group:

1645

### U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1.	5,830,986	11/03/98	Merrill, et al.	528	332	10/28/96
	2.	5,900,481	05/04/99	Lough, et al.	536	55.3	11/06/96
	3.	6,203,989	03/20/01	Goldberg, et al.	435	6	03/25/99
	4.	6,251,303	06/26/01	Bawendi, et al.	252	301.4R	09/18/98
	5.	6,277,489	08/21/01	Abbott, et al.	428	403	12/04/98
	6.	6,306,610	10/23/01	Bawendi, et al.	435	7.1	09/17/99
	7.	6,361,944	03/26/02	Mirkin, et al.	435	6	06/25/99
	8.	6,365,418	04/02/02	Wagner, et al.	436	518	05/18/00
	9.	6,417,340	07/09/02	Mirkin, et al.	536	23.1	10/20/00

### FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	10.	WO 93/25709	23 December 1993	PCT				
	11.	WO 98/04740	5 February 1998	PCT				
	12.	WO 98/17317	30 April 1998	PCT				
	13.	WO 99/60169	25 November 1999	PCT				
	14.	WO 00/33079	8 June 2000	PCT				
	15.	WO 01/00876	4 January 2001	PCT				

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	23.	WO 02/46472	13 June 2002	PCT				

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).**

	24.	Letsinger, R., et al., "Chemistry of Oligonucleotide-Gold Nanoparticle Conjugates," <i>Phosphorus, Sulfur and Silicon</i> , Volume 144, p. 359-362 (1999)
	25.	Letsinger, R., et al., "Use of a Steroid Cyclic Disulfide Anchor in Constructing Gold Nanoparticle—Oligonucleotide Conjugates," <i>Bioconjugate Chem</i> , p. 289-291 (2000)

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26.	Li Z., et al., "Multiple thiol-anchor capped DNA-gold nanoparticle conjugates," <i>Nucleic Acids Research</i> , Volume 30, p. 1558-1562 (2002)
27.	Nuzzo R., et al., "Spontaneously Organized Molecular Assemblies. 3. Preparation and Properties of Solution Adsorbed Monolayers of Organic Disulfides on Gold Surfaces," <i>J. Am Chem. Soc.</i> , Volume 109, p. 2358-2368 (1987)
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		<b>Applicant:</b> Letsinger, et al.	
		<b>Filing Date:</b> 08/04/03	<b>Group:</b> 1645

### U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date
	1.	4,193,983	3/18/80	Ullman et al.			
	2.	4,256,834	3/17/81	Zuk et al.			
	3.	4,261,968	4/14/81	Ullman et al.			
	4.	4,313,734	2/2/82	Leuvering			
	5.	4,318,707	3/9/82	Litman et al.			
	6.	4,650,770	3/17/87	Liu et al.			
	7.	4,713,348	12/15/87	Ullman			
	8.	4,853,335	8/1/89	Olsen et al.			
	9.	4,868,104	9/19/89	Kurn et al.			
	10.	5,225,064	7/6/93	Henkens et al.			
	11.	5,294,369	3/15/94	Shigekawa et al.			
	12.	5,384,073	1/24/95	Shigekawa et al.			
	13.	5,384,265	1/24/95	Kidwell et al.			
	14.	5,460,831	10/24/95	Kossofsky et al.			
	15.	5,472,881	12/5/95	Beebe et al.			
	16.	5,514,602	05/07/96	Brooks, Jr. et al.			
	17.	5,521,289	5/28/96	Hainfeld et al.			
	18.	5,543,158	8/6/96	Gref et al.			
	19.	5,571,726	11/05/96	Brooks, Jr. et al.			
	20.	5,665,582	9/9/97	Kausch et al.			
	21.	5,681,943	10/28/97	Letsinger et al.			

### OTHER DOCUMENTS - Including Author, Title, Date, Pertinent Pages, Etc.

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	22.	WO 89/06801	7/27/89	PCT				
	23.	WO 97/40181	10/30/97	PCT				
	24.	WO 98/04740	2/5/98	PCT				
	25.	WO 99/23258	10/30/98	PCT				
	26.	0 630 974 A2	12/28/94	EPO				
	27.	0 667 398 A2	8/16/95	EPO				

### OTHER DOCUMENTS - Including Author, Title, Date, Pertinent Pages, Etc.

	28.	Alivisatos et al., "Organization of 'nanocrystal molecules' using DNA," <i>Nature</i> , Vol. 382, pp. 609-611 (1996)
	29.	Bain, et al., "Modeling Organic Surfaces with Self-Assembled Monolayers," <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 28, pp. 506-512 (1989)
	30.	Bradley, "The Chemistry of Transition Metal Colloids," <i>Clusters and Colloids: From Theory to Applications</i> , G. Schmid, Editor, BCH, Weinheim, New York, pp. 459-542 (1994)
	31.	Brust et al., "Novel Gold-Dithiol Nano-Networks with Non-Metallic Electronic Properties," <i>Adv. Mater.</i> , Vol. 7, pp. 795-797 (1995)
	32.	Chen et al., "A Specific Quadrilateral Synthesized from DNA Branched Junctions," <i>J. Am. Chem. Soc.</i> , Vol. 111, pp. 6402-6407 (1989)
	33.	Chen & Seeman, "Synthesis from DNA of a molecule with the connectivity of a cube," <i>Nature</i> , Vol. 350, pp. 631-633 (1991)
	34.	Chen et al., "Crystal Structure of a Four-Stranded Intercalated DNA: d(C <sub>4</sub> ) <i>Biochem.</i> , Vol. 33, pp. 13540-13546 (1994)
	35.	Dagani, "Supramolecular Assemblies DNA to organize gold nanoparticles," <i>Chemical &amp; Engineering News</i> , p. 6-7, August 19, 1996

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36.	Dubois & Nuzzo, "Synthesis, Structure, and Properties of Model Organic Surfaces," <i>Annu. Rev. Phys. Chem.</i> , Vol. 43, pp. 437-464 (1992)
37.	Elghanian et al., "Selective Colorimetric Detection of Polynucleotides Based on the Distance-Dependent Optical Properties of Gold Nanoparticles," <i>Science</i> , Vol. 277, pp. 1078-1081 (1997)
38.	Grabar et al., "Preparation and Characterization of Au Colloid Monolayers," <i>Anal. Chem.</i> Vol. 67, pp. 735-743 (1995)
39.	Hacia et al., "Detection of heterozygous mutations in BRCA1 using high density oligonucleotide arrays and two-colour fluorescence analysis," <i>Nature Genet.</i> , Vol. 14, pp. 441-447 (1996)
40.	Jacoby, "Nanoparticles change color on binding to nucleotide target," <i>Chemical &amp; Engineering News</i> , p. 10, August 25, 1997
41.	Letsinger et al., "Use of Hydrophobic Substituents in Controlling Self-Assembly of Oligonucleotides," <i>J. Am. Chem. Soc.</i> , Vol. 115, pp. 7535-7536 (1993)
42.	Letsinger et al., "Control of Excimer Emission and Photochemistry of Stilbene Units by Oligonucleotide Hybridization," <i>J. Am. Chem. Soc.</i> , Vol. 116, pp. 811-812 (1994)
43.	Marsh et al., "A new DNA nanostructure, the G-wire, imaged by scanning probe microscopy," <i>Nucleic Acids Res.</i> , Vol. 23, pp. 696-700 (1995)
44.	Mirkin, "H-DNA and Related Structures," <i>Annu. Review Biophys. Biomol. Struct.</i> , Vol. 23, pp. 541-576 (1994)
45.	Mirkin et al., "A DNA-based method for rationally assembling nanoparticles into macroscopic materials," <i>Nature</i> , Vol. 382, pp. 607-609 (1996)
46.	Mirkin et al., "DNA-Induced Assembly of Gold Nanoparticles: A Method for Rationally Organizing Colloidal Particles into Ordered Macroscopic Materials," Abstract 249, Abstracts of Papers Part 1, 212 ACS National Meeting 0-8412-3402-7, American Chemical Society, Orlando, FL, August 25-29, 1996
47.	Mucic et al., "Synthesis and characterizations of DNA with ferrocenyl groups attached to their 5'-termini: electrochemical characterization of a redox-active nucleotide monolayer," <i>Chem. Commun.</i> , pp. 555-557 (1996)
48.	Mulvaney, "Surface Plasmon Spectroscopy of Nanosized Metal Particles," <i>Langmuir</i> , Vol. 12, pp. 788-800 (1996)
49.	Rabke-Clemmer et al., "Analysis of Functionalized DNA Adsorption on Au(111) Using Electron Spectroscopy," <i>Langmuir</i> , Vol. 10, pp. 1796-1800 (1994)

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### FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes No

### OTHER DOCUMENTS - Including Author, Title, Date, Pertinent Pages, Etc.

	50.	Roubi, "MOLECULAR MACHINES – Nanodevice with rotating arms assembled from synthetic DNA," <i>Chemical &amp; Engineering News</i> , p. 13, (Jan. 18, 1999)
	51.	Seeman et al., "Synthetic DNA knots and catenanes," <i>New J. Chem.</i> , Vol. 17, pp. 739-755 (1993)
	52.	Shaw & Wang, "Knotting of a DNA Chain During Ring Closure," <i>Science</i> , Vol. 260, pp. 533-536 (1993)
	53.	Shekhtman et al., "Stereostructure of replicative DNA catenanes from eukaryotic cells," <i>New J. Chem.</i> Vol. 17, pp. 757-763 (1993)
	54.	Smith and Feigon, "Quadruplex structure of Oxytricha telomeric DNA oligonucleotides," <i>Nature</i> , Vol. 356, pp. 164-168 (1992)
	55.	Thein et al., "The use of synthetic oligonucleotides as specific hybridization probes in the diagnosis of genetic disorders," 2 <sup>nd</sup> Ed., K.E. Davies, Ed., Oxford University Press, Oxford, New York, Tokyo, p. 21-33 (1993)
	56.	Wang et al., "Assembly and Characterization of Five-Arm and Six-Arm DNA Branched Junctions," <i>Biochem.</i> , Vol. 30, pp. 5667-5674 (1991)
	57.	Wang et al., "A DNA Aptamer Which Binds to and Inhibits Thrombin Exhibits a New Structural Motif for DNA," <i>Biochem.</i> , Vol. 32, pp. 1899-1904 (1993)
	58.	Weisbecker et al., "Molecular Self-Assembly of Aliphatic Thiols on Gold Colloids," <i>Langmuir</i> , Vol. 12, pp. 3763-3772 (1996)
	59.	Wells, "Unusual DNA Structures," <i>J. Biol. Chem.</i> , Vol. 263, pp. 1095-1098 (1988)
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<b>Examiner</b>	<b>Date Considered</b>
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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.